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APPLICATION NO	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO	CONFIRMATION NO
09/911,826	07/20/2001	Daniela Rotin	DWW-5001	9258

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CHERYL H AGRIS PHD
PO BOX 806
PELHAM, NY 10803

EXAMINER
NGUYEN, QUANG

ART UNIT	PAPER NUMBER
1636	8

DATE MAILED: 09/28/2002

Please find below and or attached an Office communication concerning this application or proceeding.

PTO-90C (Rev. 07-01)

Office Action Summary	Application No.	Applicant(s)	
	09/911,826	ROTIN ET AL.	
	Examiner	Art Unit	
	Quang Nguyen, Ph.D	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 1 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 1-35 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) _____ is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) 1-35 are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a)☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1)☐ Notice of References Cited (PTO-892)
2)☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3)☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____
4)☐ Interview Summary (PTO-413) Paper No(s) _____
5)☐ Notice of Informal Patent Application (PTO-152)
6)☐ Other

DETAILED ACTION

Claims 1-35 are pending in the present application.

Election/Restrictions

Restriction to one of the following inventions is required under 35 U.S.C. 121:

Group Restriction:

I. Claims 1-7 and 12-15, drawn to an isolated nucleic acid molecule encoding a polypeptide having GRF4 activity, an expression vector comprising the same, a transformed cell comprising the same, classified in class 536, subclass 23.1; class 435, subclass 320.1, for examples.

II. Claims 8-11 and 32-34, drawn to an isolated polypeptide having GRF4 activity and a CDC25, an isolated GRF4 polypeptide Ras activator, a recombinant GRF4 protein and a Ras binding peptide, classified in class 530, subclasses 350, 300.

III. Claims 16-18, drawn to a method for expressing a polypeptide, classified in class 435, subclass 69.1.

IV. Claim 19, drawn to a pharmaceutical comprising all or part of the polypeptide having GFR4 activity and a CDC25 domain or mimetic of the same and a pharmaceutically acceptable carrier, auxiliary or excipient, classified in class 424, subclass 94.1; class 514, subclass 2, for examples.

V. Claims 20-21, drawn to a GRF4 specific antibody, classified in class 424, subclass 130.1.

VI. Claims 22-25, drawn to a method of medical treatment of a disease, disorder or abnormal physical state characterized by excessive GRF4 expression, concentration or activity, comprising administering a product that reduces or inhibits GRF4 polypeptide expression, concentration or activity, classified in class 514, subclass 44, for example.

VII. Claims 26-28, drawn to a method of medical treatment of a disease, disorder or abnormal physical state characterized by inadequate GRF4 expression, concentration or activity, comprising administering a product that increases GRF4 polypeptide expression, concentration or activity, classified in class 514, subclass 44.

VIII. Claims 29-31, drawn to methods for identifying a compound which modulates the interaction of GRF4 with Ras or Rap1, and a method for evaluating the cell proliferation reducing properties of a compound using GRF4 or a Ras binding fragment of GRF4 or derivatives thereof with Ras or a GRF4 binding fragment of Ras or derivatives thereof, classified in class 435, subclass 7.1.

IX. Claim 35, drawn to a method for evaluating an anti-proliferative compound comprising contacting the compound with the CDC25 domain of GRF4 or a derivative thereof and determining the ability of the compound to bind, classified in class 435, subclass 7.1.

Should Applicant elect the invention of Group VI, **further group restriction is required depending on the nature or chemical structure of the product that**

reduces or inhibits GRF4 polypeptide expression, concentration or activity. Claims 22 and 25 link a plurality of patentably distinct methods of treatment using: (a) an antisense nucleic acid molecule to all or part of the nucleic acid molecule encoding a polypeptide having GRF4 activity, and (b) a product comprises all or part of Nedd4, that lack the unity of invention because the methods do not share a substantial common core structure or element among the utilized product for treatment. As set forth in MPEP 803.02, unity of invention exists if all species recited in a claim (1) shows a common utility, and (2) share a substantial structural feature disclosed as being essential to that utility. Applicant is required under 35 U.S. C 121 to elect either an antisense nucleic acid molecule to a nucleic acid molecule encoding a polypeptide having GRF4 activity as a product or a product comprising all or part of Nedd4.

The restriction requirement between linked inventions is subject to the non-allowance of the linking claims 22 and 25. The restriction requirement between linked inventions is subject to the non-allowance of the linking claim(s), 22 and 25.

Upon the allowance of the linking claims, the restriction requirement as to the linked invention shall be withdrawn and any claim(s) depending from or otherwise including all the limitations of the allowable linking claim(s) will be entitled to examination in the instant application. Applicant(s) are advised that if any such claim(s) depending from or including all the limitations of the allowable linking claim(s) is/are presented in a continuation or divisional application, the claims or the continuation or divisional application may be subject to provisional statutory and/or nonstatutory double patenting rejections over the claims of the instant application. Where a restriction

requirement is withdrawn, the provisions of 35 U.S.C. 121 are no longer applicable. See *In re Ziegler*, 44 F.2d 1211, 1215, 170 USPQ 129, 131-132(CCPA 1971). See also MPEP 804.01.

Should Applicant elect the invention of Group VII, **further group restriction is required depending on the nature or chemical structure of the product that increases GRF4 polypeptide expression, concentration or activity**. Should Applicant elect Group VII, the product in the form of a nucleic acid molecule will be examined.

The inventions are distinct, each from the other because of the following reasons:

The products of Groups I, II, IV and V are unrelated. The isolated nucleic acid molecule of Group I, the isolated polypeptide of Group II, the pharmaceutical composition of Group IV and the antibody of Group VI comprise chemically unrelated structures capable of separate manufacture, use and effect. For examples, the polypeptides and antibodies comprise unrelated amino acid sequences, and the nucleic acid molecule comprises nucleotides, distinct in chemical structure from amino acid residues. Unlike the isolated polypeptide of Group II, the pharmaceutical composition of Group IV also contains pharmaceutical acceptable carrier, auxiliary or excipient, and the intended use for the pharmaceutical composition is to attain therapeutic effects which are not required for the isolated polypeptide of Group II.

Although there are no provisions under the section for "Relationship of Inventions" in M.P.E.P. § 806.05 for inventive groups that are directed to <u>different</u> methods, restriction is deemed to be proper because the methods in Groups III, VI, VII,

VIII and IX appear to constitute patentably distinct inventions for the following reasons: These methods are directed to methods that are distinct both physically and functionally, and are not required one for the other. The method of Group III is drawn to a method for expressing a polypeptide that has nothing to do with one having GRF4 activity; the methods of Groups VI and VII require therapeutic effects in treating an individual having a disease, disorder or abnormal physical state characterized by excessive GRF4 expression, concentration or activity or an individual having a disease, disorder or abnormal physical state characterized by inadequate GRF4 expression, concentration or activity, respectively, and such therapeutic effects are not required in the screening methods of Groups VIII and Group IX. The screening methods of Groups VIII and IX, as well as methods in other Groups involve different method steps, different starting materials and different technical considerations for attaining the desired end-results.

The product of Group I is related to the methods of Groups VI and VII as product and processes of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the instant case the product of Group I can be used in the distinct process of expression a polypeptide having GRP 4 activity in an expression host system for isolation and characterization of the purified polypeptide. Furthermore, the process of Groups VI can be practiced with another materially different products, e.g. using an antibody or a

product comprising all or part of Nedd4 in the process of Group VI. It is noted that the product of Group I is not required for the making or using of any of the processes of Groups III, VIII and IX.

The product of Group II is related to the methods of Groups VII, VIII and IX as product and processes of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the instant case the product of Group II can be used in the distinct process of making a GRF specific antibody targeting to various domains of the molecule. It is noted that the product of Group II is not required for the making or using of any of the processes of Groups III and VI.

The product of Group IV is related to the method of Group VII as product and processes of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the instant case the method of Group VII can be practiced with a nucleic acid comprising all or part of the nucleic acid encoding a polypeptide having GRF4 activity. It is noted that the product of Group IV is not required for the making or using of any of the processes of Groups III, VI, VIII and IX.

The product of Group V is related to the method of Group VI as product and processes of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the instant case the process of Group VI can be practiced with an antisense molecule of the presently claimed invention or a product comprising all or part of Nedd4. It is noted that the product of Group V is not required for the making or using of any of the processes of Groups III, VII, VIII and IX.

Because these inventions are distinct for the reasons given above and have acquired a separate status in the art because of their recognized divergent subject matter, separate search requirements, it would be unduly burdensome for the examiner to search and/or consider the patentability of all the inventions in a single application. Therefore, restriction for examination purposes as indicated is proper.

Species Restriction:

Should Applicants elect Group I, claims 1, 3 and 4 are generic to a plurality of disclosed patentably distinct species comprising:

A specifically named molecule as recited in the Markush Group of claim 4.

Applicant is required under 35 U.S.C. 121 to elect a specifically named species as indicated above.

Should Applicants elect Group III, claims 16-18 are generic to a plurality of disclosed patentably distinct species comprising:

A specifically named expression host as recited in the Markush Group of claim 18.

Applicant is required under 35 U.S.C. 121 to elect a specifically named species as indicated above.

Should Applicants elect Group V, claims 20-21 are generic to a plurality of disclosed patentably distinct species comprising:

A specifically named targeted region as recited in the Markush Group of claim 20.

Applicant is required under 35 U.S.C. 121 to elect a specifically named species as indicated above.

Applicant is advised that a reply to this requirement must include an identification of the species that is elected consonant with this requirement, and a listing of all claims readable thereon, including any claims subsequently added. An argument that a claim is allowable or that all claims are generic is considered non-responsive unless accompanied by an election.

Upon the allowance of a generic claim, applicant will be entitled to consideration of claims to additional species which are written in dependent form or otherwise include all the limitations of an allowed generic claim as provided by 37 CFR 1.141. If claims

are added after the election, applicant must indicate which are readable upon the elected species. MPEP § 809.02(a).

Should applicant traverse on the ground that the species are not patentably distinct, applicant should submit evidence or identify such evidence now of record showing the species to be obvious variants or clearly admit on the record that this is the case. In either instance, if the examiner finds one of the inventions unpatentable over the prior art, the evidence or admission may be used in a rejection under 35 U.S.C. 103(a) of the other invention.

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a diligently-filed petition under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17 (h).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Quang Nguyen, Ph.D., whose telephone number is (703) 308-8339.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's mentor, Dave Nguyen, may be reached at (703) 305-2024, or SPE, Irem Yucel, Ph.D., at (703) 305-1998.

Any inquiry of a general nature or relating to the status of this application should be directed to Patent Analyst, Tracey Johnson, whose telephone number is (703) 305-2982.

Quang Nguyen, Ph.D.

DAVE T. NGUYEN
PRIMARY EXAMINER